Table 1. Exogenous and endogenous factors producing Top1 cleavage complexes

Drugs[a]	**Mechanism**[b]	**Rev**[c]	**Notes**	**Refs.**
Camptothecins	T	r	Derived from the natural alkaloid	(*196*)
Indenoisoquinolines	T	r	Synthetic; in preclinical development	(*32*)
Indolocarbazoles (NB-506)	T	r	Semi-synthetic; in clinical development	(*32*)
Actinomycin D	T	r	Other effects: DNA, RNA polymerase	(*196*)
Hoechst minor groove	T	r	Other effects: DNA	(*32*)
Ecteinascidin 743 (Yondelis^{R})	T	r	Other effects: traps TC-NER complex	(*32*)
Cytosine Arabinoside	T	r	Other effects: blocks DNA synthesis	(*197, 198*)
Gemcitabine	T	r	Other effects: blocks DNA synthesis	(*199*)
Endogenous DNA lesions				(*37, 44*)
Single base mismatches	T	r	Polymerase & mismatch defects	(*37, 40*)
Mismatched loops	T	ir	Mismatch deficiencies	(*40*)
Abasic sites	T	ir	AP sites; base excision repair	(*40*)
8-oxoguanosine	B	r	Free radicals	(*21*)
5-hydroxycytosine	?	r	Free radicals	(*21*)
Single-strand breaks	T	ir	Free radicals; base excision repair	(*41*)
Cytosine methylation	F+T	r	Physiological	(*200*)
Triple helix formation	F+T	r	?	(*201*)
Apoptotic chromatin fragmentation	B+T	ir	Appears ubiquitous during apoptosis	(*42-45*)
Exogenous DNA lesions				(*37*)
UV lesions	?	?	Dimers & 6,4-photoproducts	(*202, 203*)
IR-induced DNA breaks	T	ir	Both single- & double-strand breaks	(*41*)
0^6-methylguanine	T	r	Produced by alkylating drugs (MNNG)	(*204*)
O^6-dA-benzo[*a*]pyrene adducts	T	r	Intercalated carcinogenic adducts	(*205*)
N^2-dG-benzo[*a*]pyrene adducts	F	ir	Minor groove carcinogenic adducts	(*206, 207*)
N^2-dG-benzo[*c*]phenanthrene adducts	T	r	Intercalated carcinogenic adducts	(*207*)
N^6-Ethenoadenine	T	r	Carcinogenic vinyl adduct	(*208*)
N^2-dG-ethyl adducts	T	r	Produced by acetaldehyde (alcohol)	(*209*)

[a]: For detailed review on non-camptothecin inhibitors see (*32*).

[b]: Mechanism for Top1 cleavage complex production: T: **T**rapping of the Top1 cleavage complexes (i.e.: inhibition of religation) (see Fig. 3B); B: enhancement of binding; F: enhancement of the **f**orward (cleavage) reaction.

[c]: Reversibility of the Top1 cleavage complexes: r: reversible; ir: irreversible.